Medicines and Healthcare products Regulatory Agency

22 October 2018

CHIEF EXECUTIVE'S REPORT FOR THE MONTHS of SEPTEMBER 2018

1. HEADLINES for SEPTEMBER 2018

Brexit No-deal – The Agency (ably supported by DHSC sponsor team) has been flat-out agreeing the consultation document, impact assessment and related Statutory Instrument (SI) text, which combined will make up the consultation package. This was launched on 4th October and run for 4 weeks.
Work has also been ongoing to prioritise the tasks required to ensure the Agency will be fully operational on Brexit day 1 in the event of a No Deal outcome as part of the Business Continuity work, and a new cross-Agency working level group has been formed to coordinate this work (first meeting early October 2018).

DHSC announced New Non-Executive Director appointments to the Board. Our two new non-executive directors are Amanda Calvert and Anne-Toni Rogers. Barbara Bannister, Bruce Campbell and Stephen Lightfoot have had their appointments extended for a further three years, and Matthew Campbell-Hill, Martin Hindle, and Deborah Oakley have left the board.

Rescheduling of cannabis-based medicines –In June, the Home Secretary announced that he was commissioning a two-part review into the use of CBMPs. The first part was a therapeutic review carried out by the Chief Medical Officer (CMO). The second part was consideration of rescheduling by the Advisory Council on Misuse of Drugs (ACMD). MHRA and DHSC were tasked with developing a suitable definition to enable the necessary legislative changes to be made. MHRA, DHSC and Home Office have worked at pace to deliver this together with the necessary public health safeguards. Legislation was laid in Parliament on 11th October and subject to parliamentary scrutiny will take effect from 1st November 2018. The effect of this will be that doctors on the GMC Specialist Register will have the option to legally issue prescriptions for cannabis-based medicines when they agree that their patients could benefit from this treatment. As with other unlicensed medicines they must make decisions on prescribing cannabis-based products for medicinal use on a case by case basis, and only when the patient has an unmet special clinical need that cannot be met by licensed products. Companies producing or importing these products are subject to the established controls on the supply of unlicensed medicines. Licensing Division and IE&S have met, and will be meeting, companies that have expressed an interest in supplying these products.
We liaised with colleagues in the Home Office and DHSC on the reactive Q&A comms package ahead of the Home Office announcement. The Pharmaceutical Journal contacted us for regarding cannabis scheduling, with a focus on how the laws would work with pharmacists, doctors, and patients. We referred the journalist to DHSC. We provided guidance and our statement on products containing cannabidiol to the Eastern Daily Press and to the Daily Mail. We also directed them to the Home Office for questions on the rescheduling of cannabis for medicinal use.

Regulators Pioneer Fund – Devices made a successful bid for Pioneer funding for Devices work on developing and applying datasets for the validation of algorithms. In partnership with NHS Digital, MHRA will develop synthetic datasets to validate algorithms and artificial intelligence used in medical devices. A small group of innovators will be invited to validate their algorithms against the synthetic data as a pilot. If successful, the synthetic data sets would be made available to innovators to validate their products.

Cumberlege Review – The Terms of Reference (ToR) of the Independent Medicines and Medical Devices Safety (IMMDS) Review Group led by Baroness Cumberlege were published on 6th September on the Review website: (http://www.immdsreview.org.uk/index.html). The Call for Evidence is now open. The Agency has been invited to submit any information we consider relevant to the work of the Review that we would wish to send, and we have been asked to provide answers to a series of specific questions. A series of oral evidence gathering sessions will be held commencing in late November and will be spread out and continue into spring 2019 and we expect to receive an invitation to attend. The internal co-ordination group are working with colleagues to prepare the evidence to be submitted.

2. PRODUCT RELATED ISSUES

Medicines issues

Paraffin containing topical products and the risk of severe burns – The Commission on Human Medicines (CHM) Expert Group, set up to consider the risk of severe burns when fabric such as dressings, clothing and bedding impregnated with paraffin-containing skin creams is accidentally ignited, had its first meeting on 7 September 2018. The Group discussed the available data, options for risk minimisation and risk communication. Information has been sought from marketing authorisation holders and industry groups to support the review and the next meeting will be held in November.

Opioids and the risk of dependence, addiction and misuse – The CHM considered this issue at their September meeting and advised that an ad hoc expert group be convened to consider the current data on the utilisation of opioid-containing medicines in the UK, both prescribed and over-the-counter; to examine whether the risk minimisation measures implemented for over-the -counter and prescription opioids have been effective; to consider the benefit risk of opioid-containing medicines in particular for non-cancer indications, taking into account alternatives, and to make recommendations on appropriate regulatory action and communication. This work will be taken forward in parallel with the Public Health England review of prescribed medicines that may cause dependence or withdrawal.

Medical Device Alerts – There were four alerts in September 2018

Number	Title
MDA/2018/029	BenchMark Automated Slide Stainer series – FLO LOK III Reagent Dispenser Issue for IHC and ISH kits including INFORM HPV III Family 16 Probe (B).
MDA/2018/030	Flex connectors in Halyard Closed Suction Kits – risk of interruption of ventilation.
MDA/2018/031	SureSigns VS & VM patient monitors and Viewing stations manufactured before 3 May 2018- risk of batteries overheating or igniting.
MDA/2018/032	Various trauma guide wires – risk of infection due to packaging failure.

Clear and Simple Digital self-test pregnancy device – Healthpoint, the UK distributor for the Clear and Simple Digital self-test pregnancy device, issued a recall letter at retail level to nine customers notifying them of one specific lot which was producing a number of false positive results (leading to self-test users thinking that they were pregnant, when in fact there were not). The test kits are manufactured by Guangzhou Wondfo Biotech, and it was estimated that more than 58,000 affected tests had been distributed in the UK.

Devices issues –

- Cepheid Xpert® C.Difficile BT assay – incorrect labels applied to one batch
- Apollo Endosurgery intragastric balloon – risks of pancreatitis and spontaneous inflation.
- DXC Technology – software issue associated with the calculation of AKI from creatinine results.
- B Braun Melsungen Perfix catheter connector – leakage from or disconnection of the catheter.
- Smiths Medical – Portex thoracic catheter and connecting tube – breach of packaging seal, leading to loss of product sterility.

3. REGULATION POLICY AND OTHER SCIENTIFIC TOPICS

European/International TOPICS

International highlights

The International Coalition of Medicines Regulatory Authorities (**ICMRA)** held a face to face meeting in Washington in September. Over the three days there were key discussions focusing on Biosimilars, use of Real World Data, ensuring the patient voice is heard, regenerative medicine, increasing adverse event reporting, crisis management, communication, and the scope for future collaboration amongst ICMRA members. The secretariat is now working with members to set the strategic priorities for the next year, to complete key projects underway and to prepare presentations at forthcoming conferences.

Smart Safety Surveillance (3-S) (funded by Gates Foundation) – The 3S strategy was the theme for the International Conference of Drug Regulatory Authorities (ICDRA) meeting in Dublin during the week of 3 September, raising the profile with the international community. The MHRA are leading all work related to the bedaquiline pilot for 3S. We are in discussions with WHO as to which other countries should join the 3S bedaquiline pilot. A further meeting with the Medicines Regulatory Agency in Armenia is taking place 11-13 September to begin the delivery of the work-plan in that country. MHRA have also taken on the project management responsibilities across the entire 3S programme. New work plans for rotavirus vaccine and tafenoquine have been developed with WHO, along with country assessments for these pilots.

International Symposium of Progress on Development and Quality Control of Vaccines – Three NIBSC colleagues attended the International Symposium of Progress on Development and Quality Control of Vaccines hosted by China's National Institute for Food and Drug Control (NIFDC) in Beijing, followed by the 4th WHO Collaborating Centre network meeting for Standards held at the NIFDC.

WHO National Control Laboratory Network for Biologicals – Two NIBSC colleagues participated in the 2nd General Meeting of the WHO National Control Laboratory Network for Biologicals, which took place at the Istituto Superiore di Sanità in Rome, Italy, on 25th – 27th September. The WHO Network for Biologicals was established in 2016 by representatives from 21 national control laboratories responsible for the testing of WHO-prequalified vaccines. Since then, the network has extended to 23 full members, 6 associate members and observers (manufacturers' organisations, UN procurement agencies and other stakeholders). The network's main objectives are to share quality and technical information related to prequalified vaccines or other biological medicinal products, to facilitate recognition of the responsible national regulatory authority/control laboratory's lot release by recipient countries, thereby reducing redundant testing and promoting the

development of harmonised common standards and share best practices. The meeting was attended by representatives of the national control laboratories, WHO regions, recipient countries and two industry associations (DCVMN and IFPMA). The meeting was made possible thanks to funding from the Bill & Melinda Gates Foundation.

The International Society of Fibrinolysis and Proteolysis – Two members of the NIBSC Biotherapeutics Section attended the 24th Congress of The International Society of Fibrinolysis and Proteolysis in Edinburgh, September 3-7th. Presentations, which were also co-authored by a NIBSC colleague from Biological Imaging, were on protection of neutrophils from histones by fibrin and fibrinogen; and a proposed mechanism to explain the loss of effectiveness after treatment delay of the antifibrinolytic drug tranexamic acid used to control traumatic bleeding.

UK TOPICS

Partnership - Our work continues to build effective working relationships with relevant bodies across Government, the health sector and industry. We held a productive quarterly meeting with NICE officials on 4 September. We also convened an extraordinary meeting with the Chief Pharmaceutical Officers (CPOs) in each of the four home nations on 20 September framed around the forthcoming consultation on the Agency's Brexit no deal SIs (see Brexit section above). This was well received by the CPOs and a further such meeting is planned for late October to discuss the emerging themes from that consultation. The next regular quarterly meeting of the Cross UK Partnership Group is scheduled for 16 October and will provide a further opportunity for effective dialogue with DA colleagues on Brexit as well as discussion of other issues of common interest. The Medicines Industry Liaison Group will follow on 29 October.

Falsified Medicines Directive (FMD) implementation - The consultation closed on 23 September, with over 60 responses from a range of stakeholders. Analysis is currently ongoing.

Joint Patient Safety and Vigilance Strategy / safety messaging – We have been running a pilot to assess the impact of the electronic sending of Direct Healthcare Professional Communications (DHPCs) by the Agency. DHPCs alert healthcare professionals to changes in a medicines' use, safety profile or other change which may mean they need to review their patients who are taking it. At present these are sent by pharmaceutical companies, by post in the main. We are at the halfway stage of this pilot and have held a workshop this month to discuss the interim findings and plan the next step. We have not yet had an opportunity to pilot in primary care (it has been secondary care to date) so we are focusing on that in the second half and we are looking at the wider importance of the results in terms of presenting to our partners in the sector and what it will mean for other work looking at safety messaging.

GCMAF (Gc protein-derived macrophage activating factor) – David Noakes and his wife Lorraine Noakes unexpectedly pleaded guilty on Monday and there was coverage on ITV news as a result. Central News also requested information in relation to this. Noakes will be sentenced on 22 November. This follows a long standing enforcement investigation

Family-run Fake Pill Factory Owners – Pleads Guilty – Four people were sentenced to a total of nine years in jail at Manchester Crown Court on 7th September for the production, sale, and supply of controlled drugs, prescription only and unauthorised medicines.
This follows a lengthy investigation by colleagues in the MHRA Enforcement Group who uncovered and seized hundreds of thousands of pills, equipment and over £50,000 in cash, Rolex watches and expensive cars.

This organised criminal network operated their illicit online business from their home addresses and an office unit kitted out with hot plates, pill-pressing machine, raw ingredients and equipment to pack and distribute the products. They offered steroids, Tamoxifen, Viagra and Cialis for sale amongst other products.
The investigation established that the raw ingredients for their products were sourced from the far East and their online business stretched across Europe.
It is estimated that the total criminal benefit in this case was in the region of half a million pounds.

Action against Manufacturers of Probiotic Products – Action has been taken against several manufactures of probiotic products who have been disseminating information to health care professionals (HCP) about the use of probiotics in the treatment of a wide range of clinical conditions. The 'rationale' for this approach seems to be related to an apparent loophole in food claims legislation with companies believing that the provision of scientific information to HCP is permitted. However, the net result of this approach is that products are increasingly falling within the definition of a medicinal product. While probiotics have not typically been regarded to be borderline products in the past, there is a now a need to take appropriate action and to ensure companies are not ignorant of medicines legislation.

GCP Symposium – Almost 400 delegates attended the Agency's annual Good Clinical Practice (GCP) Symposium over two days in Leeds last week. The GCP team were joined at the symposium by 4 Food and Drug Administration (FDA) colleagues including Jean Mulinde who provided the FDA perspective on unblinding with a presentation titled 'Let me count the ways!', along with Gail Francis giving the MHRA perspective on this important issue. We were also joined by colleagues from the Brazilian authority ANVISA and the Israeli Ministry of Health, demonstrating the international appeal of our symposium.

Other topics covered in the symposium included quality systems and effective Corrective and Preventative Action (CAPA); computer system validation; a Reference Safety Information update and workshop; IMP case studies and root cause analyses; and an update on the strategic review of GCP inspections in light of new technologies in clinical trials. Immediate social media feedback was extremely positive. The symposium made for a very successful couple of days and well worth all of the hard work that the GCP team put into the event.

4. MINISTERIAL AND PARLIAMENTARY PRIORITIES

FOI Response Time Compliance: the target for 2017/18 is to ensure that 100% of requests receive responses within statutory limits (20 working days; or exceptionally within 40 days where an extension is required to complete a complex public interest test).

August 2018				
as at 31/08/2018	**FOI Requests Received 2018/2019**			
	Q1	**Jul**	**Aug**	**Total**
Received	192	66	62	**320**
Replies sent on time	190	66	61	**317**
Replies not yet due	0	0	1	**1**
Breaches	2	0	0	**2**
Compliance %	99.0%	100.0%	100.0%	**99.4%**

5. COMMUNICATION

PR and Communications Association (PRCA) national awards – We have been shortlisted for the public sector communications team of the year at the PR and Communications Association (PRCA) national awards. Our #fakemeds campaign has also been shortlisted for PRCA awards in the categories of: Health and Wellbeing, and Public Sector: Value for Money. We have also been nominated for an award from the Government Communications Service, again for the #fakemeds campaign.

Glucosamine – Next steps were identified to engage stakeholders on the change in the classification of certain glucosamine products. This will include a letter to arthritis patient groups and broader engagement on implications for the supply of food supplements for dispensing as medicines. We issued our news story confirming that, following a 2016 ruling, MHRA will consider GCPS containing doses equal to or greater than 1178mg/day of base glucosamine to be medicines. This attracted one request from a trade magazine to which we have responded.

Lidocaine – Comms provided stakeholder engagement advice in relation to reclassification of Lidocaine products, which will now only be sold under the supervision of a pharmacist. This is due to be announced in October.

Agency branding – We completed a new video for use internally and externally at events, which briefly explains the different parts of the Agency. It is also shown in our 5th floor meeting suite.

Substandard and Falsified (SF) Global Communications – We continued to work with expert contributors (Communications Working Group) of WHO to improve the global communications framework through consultation and feedback on latest version. Incorporating amendments suggested to include further detail on strategy and planning and more guidance on project planning. We presented the framework at a separate workshop event at The European Social Marketing Conference in Antwerp 6 and 7 September for critical feedback. Blending responses received with CWG contributions. We are curating latest examples of campaign materials canvassed from member states including contributions from Australia, Finland, Niger and Singapore. We are preparing to present modified framework at WHO SF Medicines Steering Group in Geneva w/c 1 October for update and feedback.

GCP Symposium – The GCP Symposium 2018 took place in Leeds on 5-6 September. The Symposium was attended by almost 400 delegates, guests and speakers over the two days. The budget for the event is still being finalised but it is projected to generate an income c.£127k and a surplus c.£89k.

FakeMeds Campaign – An update was provided to September's CET meeting on the next steps for the campaign including implementation of phase 2, costings and sponsorship plans. Following budget reductions additional scoping is underway to maximise output against agreed campaign objectives. Preparations continue at pace for the launch of phase 2, focused on STI self-test kits, to launch in early October. Significant work has been completed to develop campaign collateral, which includes new, engaging animations and static imagery that inform the audience of the risks associated with fake STI kits sold online. In addition, stakeholder communications, website edits and a press release have been developed. An internal comms piece is being drafted for publication on Insite to correspond with the launch.

Royal College of GPs (RCGP) and CPRD Quality improvement (QI) reports – we are working with RCGP on publicity about and for the RCGP annual conference 4-6 October. We are promoting the project, our workshop and attendance at the event. The next QI reports will include new indicators for prescription of anti-psychotics and anti-depressants

to adults with learning disabilities and/or autism. The reports are unique to each practice contributing data to CPRD's research database of anonymised healthcare records and support GPs to improve the clinical care of their patients.

Knowledge Transfer Partnership Programme – A news story was published on the NIBSC website and promoted on social media news of the winners of the 2018 Chief Scientific Officer's (CSO) Knowledge Transfer Partnership Programme that sees NIBSC collaborating with world class organisations and laboratories including NHS England, The National Physical Laboratory (NPL), The National Measurement Laboratory (NML) at LGC, United Kingdom Accreditation Service (UKAS) and EPSRC Fast Assessment and Treatment in Healthcare Network. The Agency is hosting 2 of the winners at NIBSC as part of this programme.

Press Communications

Pandemrix swine flu vaccine – We responded to an enquiry from the BBC into the Pandemrix swine flu vaccine, following an article in the BMJ questioning the transparency of information surrounding the safety of the swine flu vaccine. The BBC ultimately advised they were not going to run the story. We are working with VRMM colleagues on a rebuttal piece for BMJ.

Hernia Mesh – We were contacted by BBC Victoria Derbyshire show with more questions on hernia mesh. We provided answers to the journalist, ahead of the programme they did on hernia mesh on 26 September. We were contacted by BMJ and Huffington Post after the BBC programme, and provided information and comment.

Mesh Rebuttal – We corrected inaccurate statements that were made about manufacturers of mesh in a Sunday Post article.

Mesh death – We responded to BBC Online, BBC Scotland and Mail Online after vaginal mesh was mentioned as an antecedent cause on a Scottish woman's death certificate.

Diversion of Medicines – We have been continuing to speak with BBC Breakfast regarding an interview on our efforts to tackle the diversion of medicines. We also organised an interview with BBC3. Alastair Jeffreys will discuss the diversion of meds of a key demographic of younger people potentially affected by the issue. Alastair appeared on Inside Out West Midlands (BBC) discussing medicines crime and the diversion of medicines from the legal supply chain. We are also fact checking an article in Men's Health following a successful raid in Bolton covering the diversion of medicines earlier this year.

The Naked Scientists – Spanish Flu – Dr Othmar Engelhardt, Principal Scientist in the Division of Virology, flu section, NIBSC, gave an interview for a radio programme produced by The Naked Scientists, on the Spanish Flu epidemic, incorporating an exploration of the field of vaccines in the past 100 years. The show was broadcast in Cambridge on Sunday 23 September and is available as a podcast. The link to the specific work on influenza vaccines can be found at: https://www.thenakedscientists.com/articles/interviews/how-are-flu-vaccines-made

Publications

There were two papers published by Biotherapeutics this month on which Standardisation Science team members were co-authors:

"Towards international standardization of immunoassays for Müllerian inhibiting substance/anti-Müllerian hormone".

Ferguson JM, Pépin D, Duru C, Matejtschuk P, Donahoe PK, Burns CJ.
Reprod Biomed Online. 2018 Sep 5. pii: S1472-6483(18)30406-1. doi: 10.1016/j.rbmo.2018.08.012. [Epub ahead of print]

"Quantification of Müllerian Inhibiting Substance/Anti-Müllerian Hormone polypeptide by isotope dilution mass spectrometry".
Whiting G, Ferguson J, Fang M, Pepin D, Donahoe P, Matejtschuk P, Burns C, Wheeler JX.
Anal Biochem. 2018 Nov 1;560:50-55. doi: 10.1016/j.ab.2018.05.006. Epub 2018 May 6.

Two papers from Virology were published this month.

"Genetic diversity and evolution in proviral quasispecies of long term suppressed MHC-typed cynomolgus macaques".
Capone A, Lo Presti A, Sernicola L, Farcomeni S, Ferrantelli F, Maggiorella MT, **Mee ET, Rose NJ,** Cella E, Ciccozzi M, Ensoli B and Borsetti A (2018). J Gen Virol in press

"Detection by direct Next Generation Sequencing analysis of emerging enterovirus D68 and C109 strains in an environmental sample from Scotland".
Majumdar M and Martin J. (2018). Front. Microbiol. 21 August 2018 | https://doi.org/10.3389/fmicb.2018.01956

The NIBSC-authored paper of the month selected by Christian Schneider for September 2018 was chosen for demonstrating the growing research function of the Analytical and Biological Sciences (ABS) Division and for representing a positive step towards the principles of 3Rs (Replacement, Reduction, Refinement) in animal research.
Isolation and characterisation of alveolar type II pneumocytes from adult bovine lung. Lee DF, Salguero FJ, Grainger D, **Francis RJ, MacLellan-Gibson K**, Chambers MA. Sci Rep. 2018 Aug 9;8(1):11927. doi: 10.1038/s41598-018-30234-x.
This was an original research paper with the two middle authors being from NIBSC; IF 4.122
SUMMARY: Alveolar type II cells are difficult to study, partly because of currently available inefficient and expensive isolation methods. Here the authors present a new simple and cost-effective method that requires no specialist equipment to isolate bovine primary ATII cells. This isolation technique could be transferred to other species and could potentially contribute to a reduction in the number of studies requiring the use of live animals. This project was initiated by Kirsty MacLellan and Rob Francis from the Imaging section of ABS Division and was supported by an NC3Rs (National Centre for 3Rs in Research) Strategic Grant.

Other published papers considered this month had been:
Original research:
Calibration of the 7th British Working Standard for factors II, IX and X, concentrate. **Roberts G, Wilmot H, Dougall T, Rigsby P, Gray E.** Biologicals. 2018 Aug 23. pii: S1045-1056(18)30276-8. doi: 10.1016/j.biologicals.2018.08.007.

Secondary publication:
Report of the international conference on next generation sequencing for adventitious virus detection in biologicals. Khan AS, Benetti L, Blumel J, Deforce D, Egan WM, Knezevic I, Krause PR, Mallet L, Mayer D, Minor PD, Neels P, Wang G. Biologicals. 2018 Aug 6. pii: S1045-1056(18)30217-3. doi: 10.1016/j.biologicals.2018.08.002.

6. ORGANISATIONAL TOPICS

Operational Transformation – Excellent progress on the OT Programme Business Case which went to the CET and the Agency Board and was approved by both. We hit an aggressive target dealing with high volumes of complexity, building consensus across the executive and delivering a baseline for the Agency. The case is now with DHSC and the direction is being shared across the Agency. The Business Case has now been published for staff. A plan has been developed and is being implemented that seeks to ensure a managed cascade of information. The messaging ahead of publication has been to ensure staff understand what the business case is for and what to expect. Senior leaders have been provided with key messages and FAQs to ensure they are able to respond to questions from colleagues. Messages/ presentations have been prepared for the Managers' Conference, All Staff Meetings and are being prepared for the SLG on 10 October. A staff event is planned for 16 October to answer questions about the business case – for the first time this will be a live event across both our sites simultaneously by video-link and with additional facilities for staff to join remotely.

CEO meetings – On 3-5 September the CEO attended the 18th International Conference of Drug Regulatory Authorities in Dublin and spoke in a session on "Partnerships to enhance better regulatory outcomes". On 6th September the Agency held the Managers Conference in Holborn. On 7th September the CEO met with Professor Mike Kelly from the Institute of Public Health. From 10th – 12th September the CEO attended the International Coalition of Medicines Regulatory Authorities (ICMRA) Summit in Washington, hosted by the US Food and Drug Administration (FDA). Alongside the ICMRA summit, bilateral meetings were held with the FDA, with Swissmedic and with the Australian Therapeutic Goods Administration and Health Canada. On the 19th September, Dr Hudson also attended the NHS England Responsible Officer and Appraisal Network. Over 25-26 September, the Heads of Medicines Agencies (HMA) held a workshop in Copenhagen to discuss the operational aspects of the HMA, which the CEO attended.

New Policies in Human Resources - were launched in September:

- Workplace Adjustment - this is a new policy for the Agency, designed to support staff who because of disability or ill health, need reasonable adjustments in place in order to support them in work (such as equipment/changes to working hours or minor changes to the way a job is done)

We also refreshed two existing policies to include updated sources of support:

- Alcohol & Substance Abuse
- Smoke Free (including information on e-cigarettes/vaping)

Managers' Conference – nearly 250 managers attended the conference with 77 per cent saying the event was useful. Content covered included finance, Operational Transformation and managing change. A pack was sent to all managers summarising the key messages, discussion feedback, questions and responses for all agenda items.

All staff meetings - over 500 staff attended the September/ October 2018 all staff meetings at 10SC and NIBSC. In addition to the Chief Executive's usual update, there were also presentations on the Agency's financial position, Operational Transformation and Brexit. All five meetings were concluded by lively Q&A sessions where colleagues had the opportunity to ask directors questions from the floor or by means of Slido. We had no feedback from NIBSC at the time of writing as the meeting took place on 2 October, but 80% of 10SC colleagues who completed the feedback survey said they felt more or considerably more informed about the future direction of the Agency.

OPERATIONAL PERFORMANCE

New UK Marketing Authorisations (MAs) – No new active substance applications were assessed in September.

New UK Marketing Authorisations (MAs) - Existing Active Substances - The number (volume) of new MA applications assessed in September was lower when compared with the average number of assessments completed in 2017/18. The numbers of new applications determined in September was lower compared with the average monthly figures for 2017/18. (Annex - Table 1).

New UK Marketing Authorisations - Existing Active Substances September 2018

Procedure	MAA Assessed September 2018	MAA Assessed 2017/18 Average per month
National, UK-only	25	29
Decentralised, UK=RMS	8	22
Decentralised and MR, UK=CMS	30	46
Total	**63**	**97**
Procedure	**MAA Determined This Month**	**MAA Determined 2017/18 Average per month**
National, UK-only	22	18
Decentralised, UK=RMS	19	29
Decentralised and MR, UK=CMS	49	48
Total	**90**	**95**

Innovation office - The Innovation Office continues to act as a point of contact for free, consolidated advice with 15 new enquiries being received in September. As ever, the enquiries were extremely varied with requests for advice in the development of software/apps, novel medical devices and *in vitro* diagnostics, the development of medical cannabis products, pre-clinical advice for gene therapy products. In September, two teleconferences and two face-to-face meetings were held, one of which was to discuss the facilities for the manufacture of drug/device combination products. We continue to provide consolidated advice through the RASRM service. This required expertise from Licensing, Devices and Inspectorate divisions within the MHRA as well as experts from the Human Tissue Authority and Health Research Authority. Since the launch of the Innovation Office in March 2013 there have been 667 relevant queries.

Regulatory Information Service – 1092 enquiries were received in September 2018 (845 e-mails, 247 phone calls).

32 grouping requests were processed and 6 requests for expedited review were also made to LD in the month of September

Parallel imports (PLPIs) – In September, 65 PLPI initial submissions were received, 82 were assessed and 91 were determined (69, 58 and 108 respectively in August).
Median time from submission to grant was 4.9 months (6.5 months in August).
683 PLPI variation applications were received, 603 were assessed and 501 were determined (795, 697 and 711 respectively in August).
Average time from submission to grant was 2.5 months (2.0 months in August).
Training of the four new assessors is progressing well. The two scientific assessors have been accredited

Public Assessment Reports (PARs) - 100% of UK Public Assessment Reports and Lay Summaries (20/20) completed in September 2018 were published within the 60-day high-level target time from grant of the marketing authorisation. There were three updates to PARs with non-safety variation of clinical importance (Type II medical) completed in September 2018.

Clinical Trial Authorisations (CTAs) - There was a total of **75** CTA applications processed this month (*1st September* to *30th September inclusive*) with **75 (100%)** processed within the 30-day target. This included **12 (100%)** Phase 1 applications processed in an average time of **10.0** days (target 14 days).
Of all other CTAs, **63** were processed with an average time of **21.7** days and **63 (100%)** within the 30-day target.
In the calendar year to date there have been **101** Phase 1 applications processed in an average time of **12.7** days and **599** non-Phase 1 CTA applications processed in an average time of **24.8** days.
In total **463** applications have been processed in the financial year to date (**-38** compared with the same period last year).

Pharmacovigilance Adverse Drug Reactions (ADRs) – During September, the Division continued to meet all Agency targets related to the capture of ADR reports and signal detection. A total of 3036 UK ADR reports were received in September 2018, of which 856 were received from patients, parents and carers. Results against key performance measures for fatal and serious reports were both 100%; 99.8% of UK spontaneous serious ADRs were sent to EMA within the High-Level Target of 11 days and 100% of reports were sent to EMA in 12-15 days. Of 91 general enquiries received, 90% were answered within 7 working days and 10% within 10 working days.

Devices adverse incidents - 1,570 Adverse Incident reports received in September (which compares with 1,551 for the same month last year), an increase of 1.2%. The cumulative total for this year is 15,052, which compares with 13,767 for 2017, an increase of 9.3%.

Devices clinical investigations – In September 100% of clinical investigations have been completed within 60 days and the average review time for the year to date is 56 days. 9 clinical investigations were completed in September and 41 have been completed this financial year.

Biologics batch release – Test release certificates for vaccines and blood products were issued for 95 product batches in September, a decrease from the 96 issued in August. This number includes ten product batches withdrawn by the manufacturer this month. One supplementary certificate was requested this month. The target for timeliness of product testing was achieved in September. There were 243 plasma pool releases in September, a reduction from 375 in August.

7. OTHER INTERNATIONAL TOPICS

None this month.

Dr Ian Hudson
Chief Executive